DEPARTMENT OF HEALTH & HUMAN SERVICES

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CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Food and Drug Administration
Detroit District
1560 East Jefferson Avenue
Detroit, MI 48207-3179
Telephone. 313-226-6260

WARNING LETTER
2002-DT-21

January 30, 2002

Henry McKinnell, Ph.D.
President and CEO
Pfizer, Inc.
35 East 42nd Street
New York, New York 11017

Dear Dr. McKinnell:

A November 6 through December 6, 2001 inspection of your firm's aseptic drug manufacturing operations at your Terre Haute, Indiana plant found that your firm is operating in serious violation of the Federal Food, Drug, and Cosmetic Act (the Act). During the inspection, our investigators documented numerous significant deviations from the Current Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Parts 210 and 211), which cause your drug products to be adulterated within the meaning of section 501(a)(2)(B) of the Act. While some examples follow, we suggest you also refer to the list of inspectional observations which was issued at the conclusion of the inspection (copy enclosed) for additional details:

1) Failure to have a quality control unit adequate to perform its functions and responsibilities, as required by 21 CFR 211.22, as demonstrated by the number and type of inspectional observations.

2) Failure to have and to follow appropriate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile, as required by 21 CFR 211.113(b). For example:

   a. Planned interventions performed during media fills are not specifically described or enumerated in the test protocol or any related procedure.

b. In some instances, the removal of media-filled vials was not counted for contamination rate in the evaluation of acceptability of the media fill.

c. There was no justification available to assure that your current media and incubation temperatures are optimal for detecting flora that may be present in your facility.

3) Failure to have adequately designed procedures for production and process control to assure that aseptic drug products have the identity, strength, quality, and purity they purport or are represented to possess, as required by 21 CFR 211.100. For example:

a. No system was in place to assure that all personnel are monitored after exiting from the aseptic zone, or that proper procedures are followed for the monitoring of gloves and gowns.

b. Environmental monitoring limits for microbiological assessment of aseptic operations have not been defined or associated with historical counts taken in the facility. Also, personnel monitoring permits up to three organisms on gloves before any action is to be taken.

c. Production set-up time is not included in environmental monitoring of surfaces, and environmental monitoring is only performed at random intervals without any systematic means of determining 'worst case" activities for monitoring.

d. Water for injection is not sampled or evaluated at all sampling and/or use points and current points tested are only sample and tested [redacted] a week.

e. The environmental monitoring program does not include all areas immediately adjacent to aseptic operations, and which could have an adverse effect on aseptic activities.

f. No studies have been conducted to evaluate the feasibility of performing aseptic monitoring of the aseptic core area in a dynamic state rather than a resting state.

4) Failure to have separate or defined areas, or such other control systems as are necessary to prevent contamination during the course of aseptic processing operations, as required by 21 CFR 211.42(c)(10). For example:

a. The aseptic manufacturing area interfaces directly with an unclassified packaging area at the exit end for the filled, capped vials.

b. No determination has been made of the airflow at the aseptic work surface.

5) Failure to have batch production and control records which include complete information relating to the production and control of each batch, as required by 21 CFR 211.188. For example:

a. Batch production and control records for sterile products do not indicate the autoclave used for sterilization of the equipment parts and stoppers used for each production lot.

b. There is no explanation in the batch records for line stoppages that occur during aseptic vial filling, and no explanation of how the number of vials to be removed was determined when an out of limits weight check occurred.

The above list of deviations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence to each requirement of the Good Manufacturing Practice Regulations. Other Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts. Additionally, pending NDA, ANDA, or export approval requests may not be approved until the above violations are corrected.

We request that you take prompt action to correct these deviations and to ensure that your drug manufacturing systems are in full compliance with the Act and regulations promulgated thereunder. Failure to make prompt corrections may result in regulatory action without further notice, such as seizure and/or injunction.

We acknowledge receipt of Edgar M. Gray's December 21, 2001 written response to the list of inspectional observations. While Mr. Gray commits to take specific steps to correct the noted violations, we note that no commitment is made to correct any systemic weaknesses which resulted in significant deviations noted to occur in the first place, and to assure that similar deviations will not recur. We have also enclosed for your reference a copy of the FDA 483 issued on January 23, 2001, at the conclusion of an inspection of other drug manufacturing operations at your Terre Haute plant. Similarly, we acknowledge receipt of Mr. Gray's February 12, 2001 written response to that list of inspectional observations.

We expect Pfizer to globally review its operations for compliance and take appropriate corrective actions where warranted.

Please notify this office in writing, within fifteen (15) working days of your receipt of this letter, of any additional steps you have taken to correct the noted violations including an explanation of each step being taken to prevent the recurrence of similar violations. If additional corrective action cannot be completed within 15 working days, please state the reason for the delay and the time within which corrections will be completed.

Any additional correspondence should be directed to Sandra Williams, Compliance Officer, at the above address.

Sincerely yours,

Joann M. Givens
District Director
Detroit District